EXHIBIT A

IN THE UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF OHIO
EASTERN DIVISION

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IN RE: NATIONAL PRESCRIPTION OPIATE LITIGATION — MDL No. 2804

Case No. 17-md-2804
Judge Dan Aaron Polster

This Document Relates To:

The County of Lake, Ohio v. Purdue Pharma L.P., et al.
Case No. 18-op-45032

The County of Trumbull, Ohio v. Purdue Pharma L.P., et al.,
Case No. 18-op-45079

Track 3 Cases

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Remote videotaped deposition of
THERESA TOIGO

December 10, 2020
10:04 a.m.

Renee L. Pellegrino, RPR, CLR
(Appearing Remotely)

in reviewing the safety issues that may need attention post-approval. That's sort of a high-level overview.

Q. Okay. That's helpful.

Do any of those people -- and you may have said this and I just missed it. Do any of the staff that you've described get involved in evaluating the effectiveness of drugs?

A. The clinical team, so it's the medical reviewer, statistician. That's primarily who's involved in the review of the efficacy.

Q. Am I correct that the FDA is responsible in the United States for approving any drug before it can be prescribed, marketed, dispensed and sold?

A. Yes. That's FDA's responsibility.

Q. And so can a doctor prescribe a drug that has not been approved by the FDA legally?

A. No, but there are -- that's a complicated question. It's a complicated question.

MS. ARGABRIGHT: And I'm going to object for a minute because you are asking for

a legal conclusion there, and she's not a lawyer, as to FDA's legal statutory responsibilities regarding what could and could not be a drug. So, I mean, just -- she can answer, but she's not giving any legal conclusions on that.

Q. I didn't mean to ask for a legal conclusion. I'm really asking more as a practical matter. Do drugs get prescribed in this country if they have not been approved by the FDA? There may be exceptions, but as a general matter, what's the answer?

A. There's over-the-counter drugs that are often prescribed. There's prescription drugs. You know, I -- that's as best as I can answer the question. FDA reviews, approves -- reviews drugs and we approve them for marketing and we approve the labeling for the drugs.

Q. And you approve prescription drugs, branded prescription drugs, you being FDA?

A. Yes, we do, and -- yes.

Q. Does FDA also approve generic drugs?

A. Yes.

Q. And you mentioned over-the-counter drugs, FDA approves over-the-counter drugs?

A. I think that's a legal question. Over-the-counter drugs are mostly marketed under the over-the-counter monograph. FDA doesn't review each -- review an application for over-the-counter drugs.

Q. Okay. Does FDA review and approve opioids?

A. Yes.

Q. Does it review and approve benzodiazepines?

A. Yes.

Q. And does it approve -- review and approve muscle relaxers?

A. Yes.

Q. What does the FDA need to do -- what is the conclusion it needs to reach in order to approve a drug?

A. It's a benefit/risk assessment, the benefits of the drug outweigh its risks.

Q. Does it have to conclude that the drug is effective to treat whatever condition it's proposed to treat?

A. It approves that it's effective at -- for the indication approved in the labeling, yes.

Q. And where does the indication in the labeling come from, from the applicant or some other place?

A. Studies are done. FDA reviews the studies to determine whether they've met the standards for safe -- a safe and effective drug.

Q. All right. That was the other question I was going to ask you. Is part of this approval -- does part of this approval involve making a determination that the drug is safe if used as indicated on the label?

A. Yes. As described in the label, with warnings, precautions, yes.

Q. And I think you've already mentioned the risk and benefit analysis. Can you describe what that entails for the FDA to approve a prescription drug?

A. Yes.

FDA reviews the clinical data to determine that the drug is effective, and then it looks at the data that's associated with adverse events that occur during a clinical trial. It looks at where -- what therapies are available for any -- for a particular

condition. It's part of a benefit/risk assessment that is described in a document that is available, and it has a list of questions and considerations that reviewers take into account when helping to decide whether the benefits outweigh the risks.

Q. And in that process, does it consider possible side effects from the use of the drug?

A. Yes, it does.

Q. Does it consider potential interactions with other drugs?

A. It does, to the extent that they're known.

Q. Does --

A. They do describe --

Q. Sorry. Didn't mean to interrupt you.

A. They do -- those drug interactions would be described in the labeling.

Q. And does it consider potential interactions with other substances, like alcohol or perhaps other substances that somebody might take that aren't drugs?

A. Yes.

Q. Does the risk/benefit analysis consider the effects that could come from people taking the drug in ways that it was not prescribed or indicated for?

A. Yes, when -- when that's known.

Q. Does -- in the risk/benefit analysis does the FDA take into account risk to public health?

A. Yes, it does. That's part of our analysis.

Q. And are those risks -- do those risks include risks that come from inappropriate use of the drug?

A. When that's known, yes.

Q. And does it also take into account the impact on public health from the potential non-medical use of the drug?

A. When that's known, that's described in our guidance, how -- if it's known for the particular therapeutic class.

Q. And with respect to opioids in particular, does the FDA take into account these types of impacts on public health that I've just asked you about?

A. Yes, that is described in our

guidance.

Q. And on the benefit side I think you mentioned that -- some of the things that are considered, but one of them would be the conditions that the drug addresses or treats; is that right?

A. Yes.

Q. Would it also include whether there are alternative treatments available for that condition?

A. Yes.

Q. And does it consider in the risk/benefit analysis on the benefit side how effective the treatment is?

A. Can you -- can you say that question again? I'm sorry. I didn't --

Q. I'm sorry. When it's considering the benefits and weighing the risks and benefits, does it take account of how effective the drug is in treating whatever condition it's indicated for?

A. Yes. That's part of the risk/benefit determination.

Q. Does the approval also include approval of the labeling and package inserts for

a drug?

A. Yes, that's part of the approval process.

Q. And what are the components that the FDA requires in the labeling and packaging for drugs that it approves?

A. I'd have to pull out the list, but it's clinical pharmacology, pharmacology adverse -- there's a long list of adverse events, warnings, precautions, 201.56 and 57 of the CFR.

Q. Okay. Does it include information about the recommended doses?

A. Yes, it does.

Q. Okay. Does it include information about the starting dose that's recommended?

A. Yes, generally.

Q. Does it include recommendations about the duration of use of the drug?

A. Generally.

Q. And does it include information about the monitoring of the patient during the time the drug is being taken?

A. Yes.

Q. Specifically with respect to opioid

drugs, and I'm talking about as a class now, not any particular opioid drug, are all those factors part of the labeling that the FDA reviews and approves?

A. They are. The labeling is revised as FDA gets additional information, so there's labeling and approval and there's labeling at any point in time.

Q. I think you said before that one of the things or subjects that might be in a label are warnings and information from clinical trials. With respect to opioids, are warnings a part of the labeling, again, opioids as a class?

A. Yes.

Q. And is information from clinical trials with respect to any opioid also a part of the labeling?

A. Yes.

Q. If there's a general description of what kinds of -- what we mean or what you mean when you're talking about clinical information, I would appreciate it if you could tell the jury about it.

A. The labeling will describe the clinical trials that were conducted to support

the approval of the drug, so it will describe the number of trials, the patients that were included in the trials, what was found in the trials, how long the trials lasted. It will -- there will be a full description of the adverse events that were observed during the trial. If some of those adverse events are serious, they'll be described in varying levels in the labeling between warnings and precautions, adverse events, boxed warnings. It depends.

Q. What is a boxed warning?

A. A boxed warning is a -- describes a -- generally, a serious adverse event. It's one that we think -- that FDA believes that if a healthcare provider may be able to prevent an adverse event, if that's described in the labeling -- we have a guidance that describes it. I think it's three criteria. And I could find it and read it to you, but I don't know the exact three criteria. But it's the highest level of concern about a particular adverse event.

Q. The information in the label or on the label, that is available to a prescriber; is that right?

A. Yes, it is.
Q. A package insert, that's different from the label; is that also right?
A. The prescribing information is in the package insert. That's part of the labeling of the drug. A label is another piece of that component. A lawyer is probably better able to describe all of the different components of labeling, but prescribing information is a package insert, and the prescribing information is what FDA approves.
Q. And the prescribing information on the package insert is available to a prescriber who's deciding whether or not to prescribe any particular drug; is that right?
A. Yes.
Q. Including opioids?
A. Including opioids.
Q. And it's also -- I think we've all kind of gotten prescription drugs before that have a long piece of paper in it with lots of detail in it. Is that what we're talking about as a package insert?
A. No.
Q. What is that?

A. That's information for a consumer.
Q. And what kinds of information is -- well, actually, withdrawn.
Does the FDA review and approve that document?
A. No. If it's a medication guide -- if it's a medication guide, yes. Other information, no.
Q. And what is a medication guide? I just want to make sure --
A. A medication guide is when there's particular risks that FDA thinks would be important to convey to a patient, those risks are described. And, again, the specifics are described in the regulations, what's required to be included in a med guide, but it's really to help ensure the safe use of the drug for a patient. It's written -- some are better than others. You know, it's understandable language to the patient.
Q. And that medication guide, if there is one for any particular drug, is available to the patient when the patient picks up a prescription?
A. Yes.

Q. That's true for opioids as well as other drugs, other prescription drugs?

A. Yes.

Q. So would it be accurate to say that the FDA has concluded that -- and again I'm talking about the class, the class of opioids, are -- they're effective to treat the conditions that are specified in the application?

A. Yes.

Q. And the FDA has also, again, for the class of opioids, concluded that opioids are safe when used to treat the conditions that are specified in the -- on the label?

A. Yes.

Q. And they've also made the determination -- the risk/benefit determination that you've described generally before, that the risks are outweighed by the benefits?

A. Correct. No, that's not correct. You said the risks are outweighed by the benefits. The benefits outweigh the risks.

Q. Thank you for correcting me if I misspoke. So let's just make sure the record is clear on it. The FDA has made the determination that the benefits of opioids as a class outweigh

the risks that they pose?

A. That's correct.

Q. Thank you.

Now, after a drug has been approved by the FDA, I think you've already mentioned this, but there's a role that FDA has in monitoring the drug after it's on the market; is that right?

A. Yes.

Q. I think there are a number of tools that the FDA has to monitor the drug post-approval, but I wanted to ask you about a couple of them.

One of the tools that the FDA has is the FDA Adverse Event Reporting System; is that right?

A. Yes, FAERS.

Q. FAERS, right. And how does FAERS work?

A. FAERS, it's a volunteer -- healthcare practitioners submit on adverse events to FAERS. Consumers can submit adverse events to FAERS. Manufacturers are required under the regulations to submit certain adverse event reports of serious and unexpected adverse